

1, 3, 5, 23-27 and 38 have been amended herein. New claims 41-61 have been added. Upon entry of the present Amendment, claims 1, 3, 5, 12, 13, 23-27 32, 33, 35-38 and 40-61 will be pending.

As a preliminary matter, Applicants thank the Examiner for allowing time to interview the present application on August 3, 2000. It was agreed that Applicants would be able to file a declaration showing evidence of enablement following Applicants' receipt of a forthcoming Office Action. Applicants' undersigned representative called the Examiner November 3, 2000 to point out that the Examiner, despite agreeing to provide Applicants an opportunity to file such a declaration, mailed a Final Rejection. Applicants thank the Examiner for indicating that the enclosed declaration would be considered.

Applicants also enclose herewith copies of U.S. Patents 5,955,059, 5,707,648 and 5,455,335, of which Applicants' undersigned representative has recently been made aware.

#### **I. The Finality of the Office Action is Premature**

According to MPEP §706.07(b), in relevant part, the claims of a new application may be finally rejected in the first Office Action in those situations where (A) the new application is a continuing application of, or a subsequent for, an earlier application, and (B) all claims of the new application (1) are drawn to the *same invention* claimed in the earlier application. "Same invention" means identical subject matter. *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1984); *In re Ockert*, 114 U.S.P.Q. 330 (C.C.P.A. 1957); and *In re Vogel*, 164 U.S.P.Q. 619 (C.C.P.A. 1970). Applicants' amendment of claim 24 of the Preliminary Amendment, in which "miscellaneous disorders" was deleted, clearly changes the scope of the claim by deletion of an element. Two claims that differ in scope are not the "same invention." Thus, the finality of the present Office Action is premature, particularly in view of the offer by the Examiner to consider a Declaration by Applicants, as described above. Accordingly, Applicants respectfully request that the finality of the Office Action be withdrawn. In any event, because the amendments to the claims and addition of new claims remove issues for appeal (*i.e.*, rejections under §112, first and second paragraphs), Applicants respectfully request that they be entered into the record. *See*, M.P.E.P. 714.12.

**II. Double Patenting Rejections**

Claims 1-24 stand provisionally rejected under 35 U.S.C. §101 as claiming the same invention as that of claims 1-24 of co-pending application Serial No. 08/886,829. Applicants respectfully request that this rejection be deferred until allowable subject matter is indicated.

Claims 25-40 stand provisionally rejected under the doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-47 of co-pending application Serial No. 08/886,829. Applicants respectfully request that this rejection also be deferred until allowable subject matter is indicated.

**III. The Claims Are Clear And Definite**

Claims 24 and 25 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being vague and indefinite. Applicants traverse the rejection and respectfully request reconsideration in view of the amended claims.

The Office Action asserts that recitation of “biological activity against” miscellaneous disorders and diseases resulting from infection by HIV or non-retroviral viruses is vague and definite because one skilled in the art would not know how to identify the “biological activity against” an unspecified disease caused by an unspecified organism. Although Applicants disagree with the Examiner’s statements, solely to advance prosecution of the present application, Applicants have amended claim 24 to delete the objected language. Persons of ordinary skill would have no difficulty in determining whether a particular composition modulates the expression of a cellular adhesion protein or the rate of cellular proliferation.

The Office Action also asserts that recitation of “a disease or disorder that is treatable in whole or in part with one or more nucleic acids” is vague and definite because one skilled in the art would not know how to identify such a disease. Although Applicants, again, disagree with the Examiner’s statements, solely to advance prosecution of the present application, Applicants have amended claim 25 to delete the objected language. Applicants have also amended claim 25 to recite a method of “enhancing penetration of a nucleic acid across the alimentary canal of an animal” by

administering the pharmaceutical composition of claim 1, support for which can be found throughout the specification. Thus, claim 25 no longer contains any language objected to by the Examiner.

Accordingly, claims 24 and 25 are definite within the meaning of § 112. *In re Mercier*, 185 U.S.P.Q. 774 (C.C.P.A. 1975) (claims sufficiently define an invention so long as one skilled in the art can determine what subject matter is or is not within the scope of the claims). Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §112, second paragraph, be withdrawn.

#### IV. The Claimed Inventions Are Enabled

Claims 1-40 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to enable the claimed invention. Applicants traverse the rejection, as it may be applied to pending claims 1, 3, 5, 12, 13, 23-27 32, 33, 35-38 and 40-60, and respectfully request reconsideration because one skilled in the art would be able to practice the claimed inventions without being required to perform undue experimentation.

The Office Action asserts that while the specification “does provide teaching on the introduction of nucleic acids into the blood and generally into the organs of an animal via the enteric pathway,” the Office Action continues to mistakenly assert that the specification does not teach how to treat since such practice is allegedly unpredictable. The Office Action further recites several factors which purportedly support the position taken in the Office Action. The Examiner is, again, reminded that Applicants need only enable one use for such pharmaceutical compositions and that **any utility** that Applicants enable for the claimed pharmaceutical compositions is sufficient for purposes of enablement. In this respect, the Examiner’s attention is drawn to amended claim 25 which recites a method of “enhancing penetration of a nucleic acid across the alimentary canal of an animal” by administering a pharmaceutical composition of claim 1. Applicants enclose herewith a Declaration of Dr. Hardee/Dr. Teng showing that the claimed pharmaceutical compositions, in fact, enhance penetration of a nucleic acid across the alimentary canal of an animal. Paragraphs 3-5 of the Declaration describe experiments whereby penetration of an oligonucleotide across the alimentary

canal of rats and dogs is enhanced by delivery of the oligonucleotide along with at least two fatty acids. Such examples are also set forth in Applicants specification in Examples 3, 4 and 13. Thus, Applicants have clearly enabled one skilled in the art to enhance penetration of a nucleic acid across the alimentary canal of an animal by administering a pharmaceutical composition of claim 1 to the animal without requiring performance of undue experimentation. Accordingly, claim 25 is clearly enabled.


In addition, to the extent that the Examiner still takes the position that Applicants must demonstrate treatment, Applicants' previous enclosure of copies of 1) Monia *et al.*, *Nature Med.*, 1996, 2, 668, 2) Oberbauer *et al.*, *Proc. Natl. Acad. Sci. USA*, 1996, 93, 4903, 3) Monia *et al.*, *Proc. Natl. Acad. Sci. USA.*, 1996, 93, 15481, 4) Cucco *et al.*, *Cancer Res.*, 1996, 56, 4332, 5) Offensperger *et al.*, *Antisense Therapy of Hepatitis B Virus Infection*, 1996, Agrawal Ed., Humana Press Inc. Tolowa, NJ, pp. 143-158, 6) Sun *et al.*, *Br. J. Pharmacol.*, 1996, 118, 131, 7) Neurath *et al.*, *Nature Med.*, 1996, 2, 998-1004, 8) Leonetti *et al.*, *J. N.C.I.*, 1996, 88, 419, and 9) Del Bufalo *et al.*, *Br. J. Cancer*, 1996, 74, 387, contrary to the assertions in the Office Action, provides a nexus between the successful enhancement of oligonucleotide penetration across the alimentary canal in an animal and treatment of an animal. Indeed, each reference demonstrates successful administration of pharmaceutical nucleic acids via the bloodstream or local administration. Each of these references shows that oligonucleotides administered to the bloodstream, in fact, reach their target destinations as well as have their intended effects on the target. Since the Office Action admits that Applicants have enabled one skilled in the art to "introduce nucleic acids into the blood and generally into the organs of an animal via the enteral pathway," and since the state of the art at the time the application was filed demonstrates that oligonucleotides administered into the blood reach their intended target and have, for example, anti-tumor activity, an appropriate nexus to treatment has been established. Further, since nucleic acids have been shown to have at least some therapeutic value, pharmaceutical compositions comprising penetration enhancers and the nucleic acids are also enabled. Thus, one skilled in the art is not required to perform any amount of undue experimentation in order to practice the claimed invention.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph, be withdrawn.

**V. Conclusion**

It is respectfully submitted that this application is now in condition for allowance. Accordingly, an indication of allowability and an early Notice of Allowance are respectfully requested.

Respectfully submitted,

  
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